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Dec 29, 1998

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TITLE: Composition and method for delivery of nucleic acids

DATE-ISSUED: December 29, 1998

INVENTOR-INFORMATION:

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US-CL-CURRENT: 514/44; 435/6, 554/224, 554/80, 560/155, 560/224, 560/252

CLAIMS:

We claim:

1. A method for introducing nucleic acid into a cell comprising exposing the cell to a compound having the formula: ##STR5## in which: w is a nucleic acid x is a non-amino acid or non-peptide binding group y is a spacer having a chain length equivalent to 1-30 carbon-carbon single covalent bonds or is absent R.sub.4 is H or halogen or CH.sub.2 O--R.sub.3 ; and R.sub.1, R.sub.2 and R.sub.3 are the same or different and are either hydrogen, methyl, ethyl, alkyl, alkenyl, hydroxylated alkyl, hydroxylated alkenyl groups or ether containing alkyl, alkenyl, hydroxylated alkyl or hydroxylated alkenyl groups, optionally being an acyl group derived from a fatty acid having a carbon chain length equivalent to 3-24 carbon atoms saturated or unsaturated, with the proviso that at least one of R.sub.1, R.sub.2 or R.sub.3 includes a group having a carbon chain of 3-24 carbon atoms saturated or unsaturated.
2. A method as claimed in claim 1 in which y is present.
3. A method as claimed in claim 1 in which the nucleic acid is DNA, RNA or oligonucleotides of either DNA or RNA, modified oligonucleotides or a combination thereof.
4. A method as claimed in claim 1 in which R.sub.1, R.sub.2 and R.sub.3 are the same.
5. A method as claimed in claim 1 in which R.sub.1, R.sub.2 and/or R.sub.3 are cholesterol or acyl derivatives of fatty acids selected from the group consisting of palmitate, myristate, laurate, caprate and oleate.
6. A method as claimed in claim 5 in which R.sub.1, R.sub.2 and/or R.sub.3 are acyl derivatives of myristate or laurate.
7. A method as claimed in any claim 1 in which the cells are animal cells.
8. A method as claimed in claim 1 in which the cells are plant cells.
9. A method as claimed in claim 7 in which the method is conducted in vitro.
10. A method as claimed in claim 7 in which the method is conducted in vivo.
11. A method as claimed in claim 10 in which the compound is administered topically, intravenously, intramuscularly, by inhalation, injection, orally or by suppository.
12. A method as claimed in claim 1 in which the compound is present in a liposome or mixed with another lipid.
13. A method as claimed in claim 1 in which the compound contains a spacer group

- "y" having a chain length equivalent to 3 to 17 carbon atoms.
14. A method as claimed in claim 13 in which y is amino butyric, amino caproic, amino caprylic or amino undecanoic acid or a dipeptide of amino caproic acid and amino undecanoic acid.
15. A method as claimed in claim 1 in which x has an overall positive charge and the nucleic acid is associated electrostatically.
16. A method as claimed in claim 1 in which x is an oligonucleotide and nucleic acid w is associated with x by base pairing or triple helix formation.
17. A method as claimed in claim 1 in which w is covalently attached to x.
18. A method as claimed in claim 1 in which w is associated to x by hydrogen bonding.
19. A method for introducing nucleic acid into a cell comprising exposing the cell to a compound having the formula:
- w . . . x--y--NH--CH.sub.2 --CH.sub.2 O--R.sub.5
- in which:
- w is a nucleic acid
- x is a non-amino acid or non-peptide binding group
- y is a spacer having a chain length equivalent to 1-30 carbon-carbon single covalent bonds or is absent
- R.sub.5 is alkyl, alkenyl, hydroxylated alkyl, hydroxylated alkenyl group or ether containing alkyl, alkenyl, hydroxylated alkyl or hydroxylated alkenyl group, optionally being an acyl group derived from a fatty acid having a carbon chain length equivalent to 3-24 carbon atoms saturated or unsaturated, with the proviso that R.sub.5 includes a group having a carbon chain of 3-24 carbon atoms saturated or unsaturated.
20. A method as claimed in claim 19 in y is present.
21. A method as claimed in claim 19 in which the nucleic acid is DNA, RNA or oligonucleotides of either DNA or RNA, modified oligonucleotides or a combination thereof.
22. A method as claimed in claim 19 in which R.sub.5 is cholesterol or an acyl derivative of a fatty acids selected from the group consisting of palmitate, myristate, laurate, caprate and oleate.
23. A method as claimed in claim 22 in which R.sub.5 is an acyl derivative of myristate or laurate.
24. A method as claimed in claim 19 in which the cells are animal cells.
25. A method as claimed in claim 19 in which the cells are plant cells.
26. A method as claimed in claim 24 in which the method is conducted in vitro.
27. A method as claimed in claim 24 in which the method is conducted in vivo.
28. A method as claimed in claim 27 in which the compound is administered topically, intravenously, intramuscularly, by inhalation, injection, orally or by suppository.
29. A method as claimed in claim 19 in which the compound is present in a liposome or mixed with another lipid.
30. A method as claimed in claim 19 in which the spacer group "y" has a chain length equivalent to 3 to 17 carbon atoms.
31. A method as claimed in claim 30 in which y is amino butyric, amino caproic, amino caprylic or amino undecanoic acid or a dipeptide of amino caproic acid and amino undecanoic acid.
32. A method as claimed in claim 19 in which x has an overall positive charge.
33. A method as claimed in claim 19 in which x is an oligonucleotide and nucleic acid w is associated with x by base pairing or triple helix formation.
34. A method as claimed in claim 19 in which w is covalently attached to x.
35. A method as claimed in claim 19 in which w is associated to x by hydrogen bonding.
36. A compound for use in introducing nucleic acid into a cell, the compound having the formula ##STR6## in which: w is a nucleic acid
- x is a non-amino acid or non-peptide binding group
- y is a spacer having a chain length equivalent to 1-30 carbon-carbon single covalent bonds or is absent
- R.sub.4 is H or halogen or CH.sub.2 O--R.sub.3 ; and R.sub.1, R.sub.2 and R.sub.3 are the same or different and are either hydrogen, methyl, ethyl, alkyl, alkenyl, hydroxylated alkyl, hydroxylated alkenyl groups or ether containing alkyl, alkenyl, hydroxylated alkyl or hydroxylated alkenyl groups, optionally being an acyl group derived from a fatty acid having a carbon chain length equivalent to 3-24 carbon atoms saturated or unsaturated, with the proviso that at least one of R.sub.1, R.sub.2 or R.sub.3 includes a group having a carbon chain of 3-24 carbon atoms saturated or unsaturated.
37. A compound as claimed in claim 36 in which y is present.
38. A compound as claimed in claim 36 in which w is DNA, RNA or oligonucleotides

- of either DNA or RNA, modified oligonucleotides or a combination thereof.
39. A compound as claimed in claim 36 in which R.sub.1, R.sub.2 and R.sub.3 are the same.
40. A compound as claimed in claim 36 in which R.sub.1, R.sub.2 and/or R.sub.3 are cholesterol or acyl derivatives of fatty acids selected from the group consisting of palmitate, myristate, laurate, caprate and oleate.
41. A compound as claimed in claim 40 in which R.sub.1, R.sub.2 and/or R.sub.3 are acyl derivatives of myristate or laurate.
42. A compound as claimed in claim 36 in which the compound is present in a liposome or mixed with another lipid.
43. A compound as claimed in claim 36 in which the compound contains a spacer group "y" having a chain length equivalent to 3 to 17 carbon atoms.
44. A compound as claimed in claim 43 in which y is amino butyric, amino caproic, amino caprylic or amino undecanoic acid or a dipeptide of amino caproic acid and amino undecanoic acid.
45. A compound as claimed in claim 36 in which x has an overall positive charge.
46. A compound as claimed in claim 36 in which x is an oligonucleotide and nucleic acid w is associated with x by base pairing or triple helix formation.
47. A compound as claimed in claim 36 in which w is covalently attached to x.
48. A compound as claimed in claim 36 in which w is associated to x by hydrogen bonding.
49. A compound for use in introducing nucleic acid into a cell, the compound having the formula:
w . . . x--y--NH--CH.sub.2 --CH.sub.2 O--R.sub.5
in which:
w is a nucleic acid
x is a non-amino acid or non-peptide binding group
y is a spacer having a chain length equivalent to 1-30 carbon-carbon single covalent bonds or is absent
R.sub.5 is alkyl, alkenyl, hydroxylated alkyl, hydroxylated alkenyl group or ether containing alkyl, alkenyl, hydroxylated alkyl or hydroxylated alkenyl group, optionally being an acyl group derived from a fatty acid having a carbon chain length equivalent to 3-24 carbon atoms saturated or unsaturated, with the proviso that R.sub.5 includes a group having a carbon chain of 3-24 carbon atoms saturated or unsaturated.
50. A compound as claimed in claim 49 in which y is present.
51. A compound as claimed in claim 49 in which w is DNA, RNA or oligonucleotides of either DNA or RNA, modified oligonucleotides or a combination thereof.
52. A compound as claimed in claim 49 in which R.sub.5 is cholesterol or an acyl derivative of a fatty acids selected from the group consisting of palmitate, myristate, laurate, caprate and oleate.
53. A compound as claimed in claim 52 in which R.sub.5 is an acyl derivative of myristate or laurate.
54. A compound as claimed in claim 49 in which the compound is present in a liposome or mixed with another lipid.
55. A compound as claimed in claim 49 in which the compound contains a spacer group "y" having a chain length equivalent to 3 to 17 carbon atoms.
56. A compound as claimed in claim 55 in which y is amino butyric, amino caproic, amino caprylic or amino undecanoic acid or a dipeptide of amino caproic acid and amino undecanoic acid.
57. A compound as claimed in claim 49 in which x has an overall positive charge.
58. A compound as claimed in claim 49 in which x is an oligonucleotide and nucleic acid w is associated with x by base pairing or triple helix formation.
59. A compound as claimed in claim 49 in which w is covalently attached to x.
60. A compound as claimed in claim 49 in which w is associated to x by hydrogen bonding.
61. A method according to claim 1, wherein the dotted line between w and x denotes the bonding association of w and x in the compound.
62. A method according to claim 1, wherein the nucleic acid group w can associate with the non-amino acid or non-peptide group x by covalent bonding, ionic interaction, hydrogen bonding, base pairing or triplex formation.

FILE 'MEDLINE' ENTERED AT 07:58:43 ON 26 JAN 2001
L1 4 S SUPPOSITORY AND IMMUNE RESPONSE

FILE 'STNGUIDE' ENTERED AT 08:00:19 ON 26 JAN 2001

FILE 'CAPLUS, EMBASE, BIOSIS' ENTERED AT 08:03:30 ON 26 JAN 2001
L2 11 S L1
L3 10 DUP REM L2 (1 DUPLICATE REMOVED)

FILE 'MEDLINE' ENTERED AT 08:06:45 ON 26 JAN 2001
L4 0 S TRANSFEC? AND RECTAL AND SUPPOSITORY
L5 0 S TRANSFEC? AND SUPPOSITORY
L6 3657 S SUPPOSITORY
L7 20 S L6 AND (PLASMID OR NUCLEIC OR DNA OR VECTOR OR ?VIRUS)

FILE 'CAPLUS, EMBASE, BIOSIS' ENTERED AT 08:18:25 ON 26 JAN 2001
L8 218 S L7
L9 203 DUP REM L8 (15 DUPLICATES REMOVED)
L10 114 S L9 AND IMMUN?
L11 18 S L10 AND (PLASMID OR VECTOR OR NUCLEIC)

(FILE 'HOME' ENTERED AT 09:47:22 ON 26 JAN 2001)

FILE 'MEDLINE' ENTERED AT 09:47:38 ON 26 JAN 2001
L1 134 S GENETIC IMMUNIZ?
L2 1 S L1 AND (GASTROINTESTINAL OR COLON OR INTESTINE OR JEJUNUM OR
L3 251 S TRANSFEC? AND (GASTROINTESTINAL OR COLON OR INTESTINE OR JEJ
L4 12 S L3 AND IMMUNIZ?

S #

Updt

Database

Query

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Comment

S1417

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USPT

genetic immunization and
(suppository.clm.)

2001-01-26

09:02:29

S1416

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USPT

suppository.clm. and nucleic.clm.

2001-01-26

08:28:41

S1415

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USPT

henning.in. and intestine.ti.

2001-01-26

08:25:43

S1414

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USPT

genetic immunization and suppository

2001-01-26

07:46:43

S1413

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USPT

5674703.pn. and antigen

2001-01-26

07:41:24

S1412

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5674703.pn.

2001-01-26

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S1411

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USPT

yoshida tumor virus

2001-01-25

12:23:57